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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,124	11/13/2003	Victoria Smith	P2000R1	7683

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EXAMINER	
QIAN, CELINE X	
ART UNIT	**PAPER NUMBER**
1636	

MAIL DATE	DELIVERY MODE
08/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/712,124	SMITH, VICTORIA	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,9,10,12-18 and 25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,9,10,12-18 and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3, 4, 6, 9, 10, 12-18, 25-30 are pending in the application.

This Office Action is in response to the Amendment filed on 6/1/07.

Response to Amendment

The rejection of claims 3, 10, 14-27 under 35 U.S.C. 112 2nd paragraph have been withdrawn in light of Applicant's amendment.

The rejection of claims 1, 3, 4, 6, 9, 10, 12-18, 25-30 under 35 U.S.C. 112 1st paragraph has been maintained for reason set forth of the record mailed on 12/14/06 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full; clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 4, 6, 9, 10, 12-18, 25-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In response to this rejection, Applicants assert the amendment now reciting "naturally occurring variant," and the specific sequences of SEQ ID NO: 3, 13, 17, 23 and 43 are clearly representative of the narrow genera of the sequences and their naturally occurring variants, such

as allelic and splice variants. Applicants thus conclude that the Applicants have possession of the claimed invention.

The above arguments have been fully considered but deemed unpersuasive. The reasons for lack of adequate description of the claimed variants were set forth in detail in the office action mailed on 12/14/07. In response to the above argument, although the claimed genus of variants are narrowed to naturally occurring variants of the SEQ ID NO: 3, 13, 17, 23 and 43, the specification still fails to demonstrate any of such naturally occurring variants may be substituted in determining the whether the patient have HGD. Although natural variants such as allelic or splice variants may be identified by known method, the method for identifying said variants cannot be used to substitute the actual description of said variants and their relationship in determining HGD. Moreover, according to the specification (page 15, lines 10-12), the naturally occurring variants also encompass sequence variants which may not even function as the sequence disclosed as SEQ ID NO: 3, 13, 17, 23 and 43. For such broadly claimed genus, the specification fails to describe a representative number of species by their complete structure or the relationship between the claimed variants with their prediction value in the case of HGD. Therefore, for reasons set forth in the previous office action and above, this rejection is maintained.

Claims 1, 3, 4, 6, 9, 10, 12-18, 25-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to this rejection, Applicants argue that the claimed method is directed to detecting hyperplasia in esophagus or colon tissue by determining the expression of the five recited gene. Applicants assert that the teaching of Kroese and Lucentini do not apply because the reference addresses the issues in the genetic test, whereas the claimed method does not belong to such genetic test. Further, Applicants argue that Shalon et al. do not represent state of the art at the time the invention was made because it was written in 1995. Applicants assert that 2 fold increase is not required in the current invention because statistical significance is also a function of sensitivity of the technique and equipment used for gene expression profiling. Moreover, Applicants assert that the sampled assayed in the current invention is sufficient in number to have statistical significance. Lastly, Applicants assert that the result in Example 3 are result from rigorous analysis, including calculation of standard deviation and normalization, and as discussed in Example 4, genes with elevated expression are identified as those with Z scores of >1.7 in the disease group. Applicants thus conclude that the claimed invention is enabled by the instant specification.

The above arguments are fully considered but deemed unpersuasive. The reasons for the lack of enablement of the instantly claimed invention is set forth in detail in the office action mailed on 12/14/07. In response to the arguments with regard to Kroese and Lucentini, the examiner does not agree that the teaching of Kroese and Lucentini does not apply to the instantly claimed invention. The comments about heterogeneous nature of the genetic condition may not be relevant in the instant case, however, the discussion about the complexity of testing also applies to the instant claimed invention. It appears that Applicants are taken the statements on page 475, 2nd col. from the article out of context. Immediately following the sentence defining

the "genetic test," Kroese et al. went on to say that "there are many problems and issues that surround this definition. For our purposes, we focus on the concept of a gene test, defining that as one based on the analysis of human DNA using a variety of different technologies...We also note that a test may seek to predict or determine the susceptibility to, or probability of developing disease in the future, as well as establish a diagnosis in someone with clinical signs and symptoms." The instant claims are drawn to a method detecting a disease (HGD) based on the increased expression of 5 different genes. Although the test is not based upon analyzing the DNA sequence per se, the gene expression is measured. The claimed subject matter clearly falls within the scope of the review that the author intended to cover. Similarly, with respect to Lucentini, this reference teaches the association of gene studies with specific disease needs to be confirmed because most first reports turn out to be not reliable. Such teaching reflects the unpredictability in the relevant field of genetic testing.

With respect to the teaching of Shalon, Applicants are mistaken that this publication is filed on 1995, in fact, this application is filed on 7/17/2001. In response to Applicants' argument from the statistical significance, the teaching disclosed in on page 8 indicates that tissues with HGD from only 3 patients (the claims are directed to identify HGD, not intermediate or low grade hyperplasia) were analyzed and whereas the normal control are from 10 normal individuals. With the small sample size, and without the confirmation of the test results by a different method such as quantitative PCR, it hardly indicates that the results are statistically significant enough to be used as a genetic test for identifying HGD. Moreover, as discussed in the previous office action, other factors not related to HGD also affect the expression of the genes. In view of the level of high unpredictability in the art of genetic testing, and the limited

teaching from the specification, the claimed method is not enabled. Therefore, this rejection is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELINE QIAN, PH.D.
PRIMARY EXAMINER